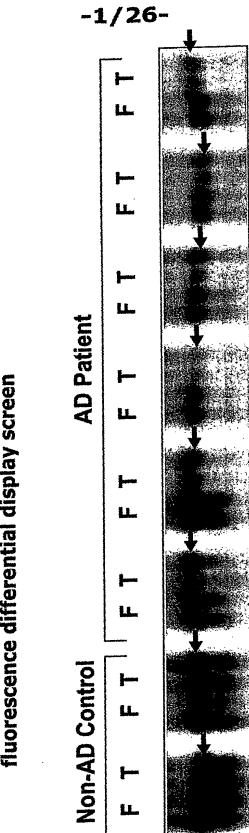
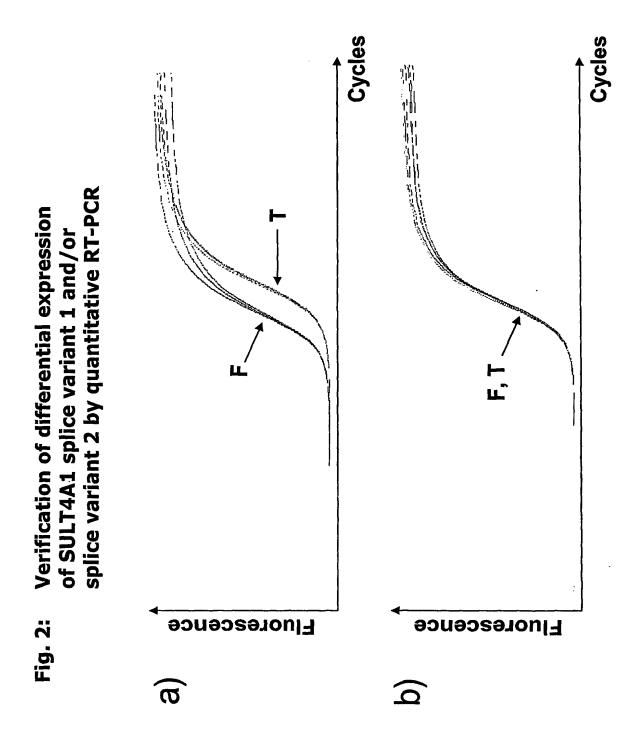
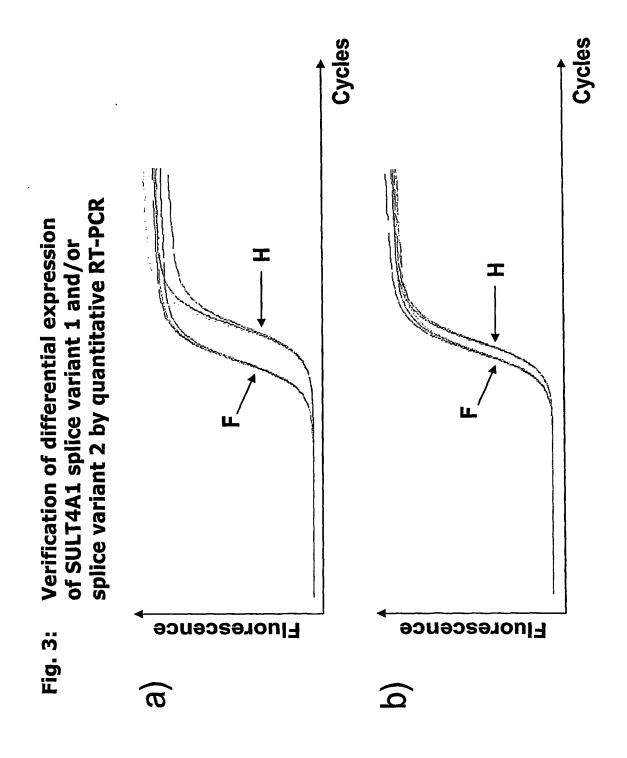
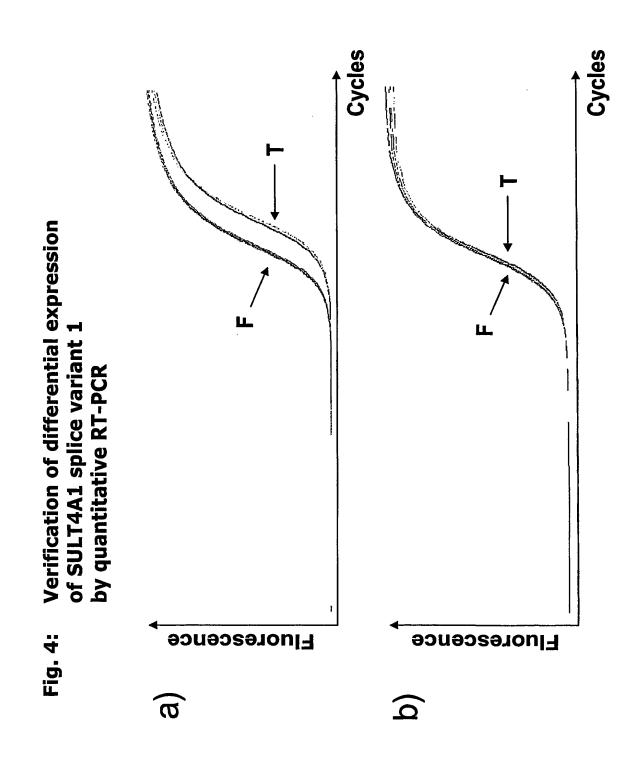
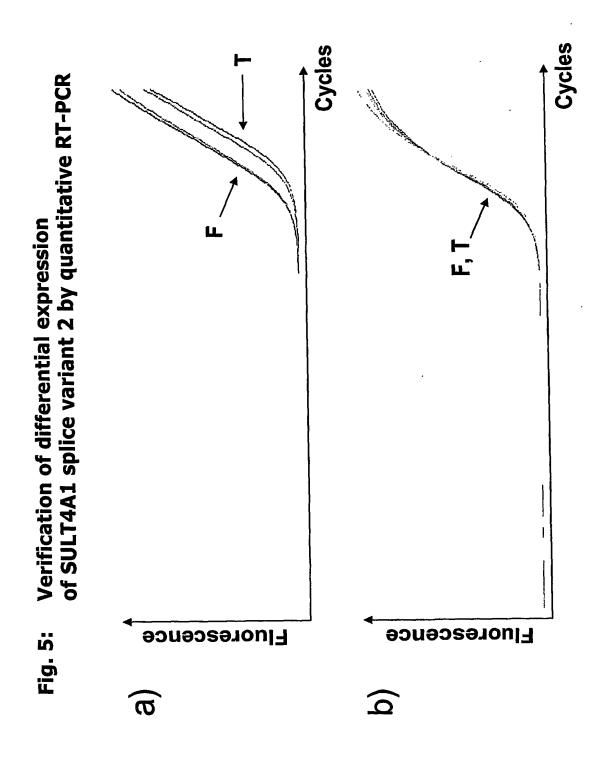
Fig. 1: Identification of differentially expressed genes in a fluorescence differential display screen











Comparison of Braak 0-1 with 2-3 and 4-6

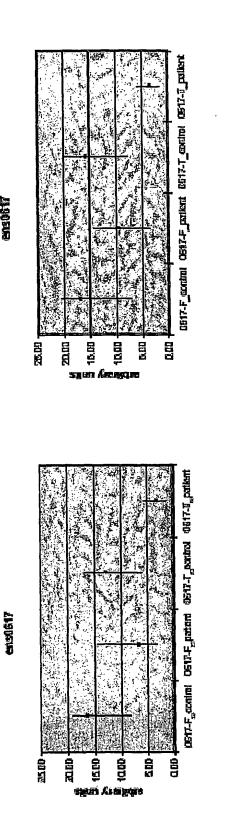
Compatison of Break 0-1 with 2-6

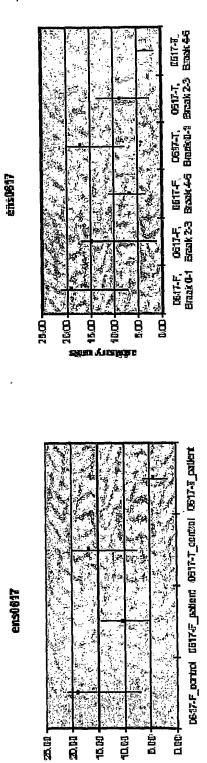
expression of SULT4A1sv1 and/or SULT4A1sv2 Fig. 6: Analysis of absolute mRNA

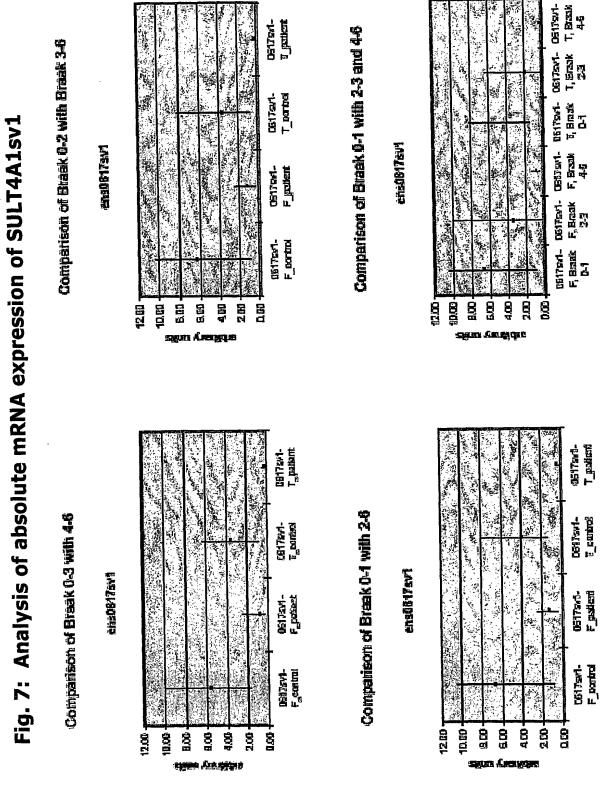
Companison of Break 0-3 with 4-5

Comparison of Braak 0-2 with Braak 3-6

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Fig. 8: SEQ ID NO. 1: amino acid sequence of human SULT4A1 protein, splice variant 1

Length: 284 aa

1	MAESEAETPS	TPGEFESKYF	EFHGVRLPPF	CRGKMEEIAN	FPVRPSDVWI
51	VTYPKSGTSL	LQEVVYLVSQ	GADPDEIGLM	NIDEQLPVLE	YPQPGLDIIK
101	ELTSPRLIKS	HLPYRFLPSD	LHNGDSKVIY	MARNPKDLVV	SYYQFHRSLF
151	TMSYRGTFQE	FCRRFMNDKL	GYGSWFEHVQ	EFWEHRMDSN	VLFLKYEDME
201	RDLVTMVEQL	ARFLGVSCDK	AQLEALTEHC	HQLVDQCCNA	EALPVGRGRV

251 GLWKDIFTVS MNEKFDLVYK QKMGKCDLTF DFYL

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Fig. 9: SEQ ID NO. 2: amino acid sequence of human SULT4A1 protein, splice variant 2

Length: 171 aa

1 MAESEAETPS TPGEFESKYF EFHGVRLPPF CRGKMEEIAN FPVRPSDVWI

51 VTYPKSVGYG SWFEHVQEFW EHRMDSNVLF LKYEDMHRDL VTMVEQLARF

101 LGVSCDKAQL EALTEHCHQL VDQCCNAEAL PVGRGRVGLW KDIFTVSMNE

151 KFDLVYKQKM GKCDLTFDFY L

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Fig. 10: SEQ ID NO. 3: nucleotide sequence of human SULT4A1 cDNA, splice variant 1

Length: 2419 bp

_					ar acadaar aa
1				GCGAGGCCGA	
51			CAAGTACTTC		
101	GCCGCCCTTC		AGATGGAGGA		TTCCCGGTGC
151	GGCCCAGCGA	CGTGTGGATC			CACCAGCTTG
201	•	TGGTCTACTT	GGTGAGCCAG		CCGATGAGAT
251		AACATCGACG		GGTCCTGGAG	
301		CATCATCAAG		CTCCCCGCCT	CATCAAGAGC
351	CACCTGCCCT	ACCGCTTTCT	GCCCTCTGAC	CTCCACAATG	
401			ACCCCAAGGA		TCTTATTATC
451	AGTTCCACCG	CTCTCTGCGG	ACCATGAGCT	ACCGAGGCAC	CTTTCAAGAA
501	TTCTGCCGGA	GGTTTATGAA	TGATAAGCTG	GGCTACGGCT	CCTGGTTTGA
551	GCACGTGCAG	GAGTTCTGGG	AGCACCGCAT	GGACTCGAAC	GTGCTTTTTC
601	TCAAGTATGA	AGACATGCAT	CGGGACCTGG	TGACGATGGT	GGAGCAGCTG
651	GCCAGATTCC	TGGGGGTGTC	CTGTGACAAG	GCCCAGCTGG	AAGCCCTGAC
701	GGAGCACTGC	CACCAGCTGG	TGGACCAGTG	CTGCAACGCT	GAGGCCCTGC
751	CCGTGGGCCG	GGGAAGAGTT	GGGCTGTGGA	AGGACATCTT	CACCGTCTCC
801	ATGAATGAGA	AGTTTGACTT	GGTGTATAAA	CAGAAGATGG	GAAAGTGTGA
851	CCTCACGTTT	GACTTTTATT	TATAATAACA	GAAACAACAA	CCTGCATGCT
901	CACAATACCC	AGACAGTCTA	CTAGCCAAAA	GTCCTGTATG	CATTCATTTA
951	TTCCTTGCTG	GACAAACTCT	GGAAGCAGCG	TGTGAAACAG	CGGGGGAAGG
1001	GAAGAGCGGC	GTGAGCGGAG	GGAGTGTGAT	GATTCCCAAC	CGAAGCAGCT
1051	GTCTCGCCTT	TAGAACGTGC	AGCCTCTCCA	TGTCTGATTA	CAAACAGTCT
1101	CCACATTGCA	GTTCCAATGG	CCTGGACCGT	AAGGATAAAG	CCTGTAATAT
1151	ATGCAACTAG	AATGTCTGCC	TTTTCAACCC	CGTATTATTG	TATTTTATAG
1201	AGCTTTTCAC	TGGAAATCTA	CATAAATGTC	AGTAAACCAA	ATAAAAGTTC
1251	ATTTCCAAGG	GGAATCAGGA	GCGAGCCACA	CCCGAATGGT	AGAAAGATCT
1301	CAGGGTTAAC	TCTTTATTTT	TGTAGTTTTA	TTATCTAAGG	CACAGCCATT
1351	CTGTTCTCAC	TTGGTTCTGA	GATAGTGGTG	AGAACAGAGG	ATGAGTTGGG
1401	TCTGTTGGGG	GGAATCTGGA	CACTTGTTTA	TTCTGACGGA	GTTCACTTCT
1451	TCAGAACCTT	CCTGAAATGA	GCAGAAATTG	TTCACTAGGT	CTTCAGAATG
1501	GACGTCCTTC	TGCCAGAGAC	TTCCAGCGGG	CGGCTCCAAA	GGCCCAATGC
1551	AGAGGAGCCC	GCGGAGCATG	TGCTGAGGGA	AGTCTGCCTG	GTGAGGCTGG
1601	CAGGTGGGAG	TCTAATGCAG	TCAGGAGCAT	TTGCATGCAG	TGGGTGGAGA
1651	GTCGGCCACC		GTTGCGCTCG	GAATTTGAGC	TGAATTCCAC
1701	AGCCTTACTT	•	AGTGATAGCC	TACTAATGCT	GGCAAGCAGA
1751	TGCTTAATAG		AAATCCCCGG	GTCTTTATCA	TTCAGTTTGT
1801	TCTGTGCACC				
1851	CCCTGTTTCA		GTTGGCACGG	- -	
1901	CTCATCCCTC		AGGGAGTAAA		
1951	ACTGCCTAAT		- - ·	AAGCGATGGA	
2001			TGGGGACCGG		
2051				GGGTCGCTGC	
202I	GCIGGWMGC	. ACCCUMMGIG	G TOG T CHOOM		DDDARDULLL

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2101	GTCTCCGTTC	TTGGTGCTGT	ATTTGAAACG	GGTGTAGAGA	GAAGCTTGTG
2151	TTTTTGTTTG	TAATGGGGAG	AAGCGTGGCC	AGGCAGGTGG	CACGTGGCAT
2201	CGCATGGTGG	GCTCGGCAGC	ACCTTGCCTG	TGTTTCTGTG	AGGGAGGCTG
2251	CTTTCTGTGA	AATTTCATTT	ATATTTTTCT	ATTTTTAGTA	CTGTATGGAT
2301	GTTACTGAGC	ACTACACATG	ATCCTTCTGT	GCTTGCTTGC	ATCTTTAATA
2351	AAGACATGTT	CCCGGCGTTG	CAAAAAAAAA	AAAAAAAAA	AAAAAAAAA
2401	AAAAAAAAA	AAAAAAAA			

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Fig. 11: SEQ ID NO. 4: nucleotide sequence of human SULT4A1 cDNA, splice variant 2

Length: 2080 bp

1	GCGACGGCGA	CGGCGGCGGC	ATGGCGGAGA	GCGAGGCCGA	GACCCCCAGC
51	ACCCCGGGGG		CAAGTACTTC	GAGTTCCATG	· ·
101	GCCGCCCTTC	TGCCGCGGGA	AGATGGAGGA	GATCGCCAAC	TTCCCGGTGC
151	GGCCCAGCGA	CGTGTGGATC	GTCACCTACC	CCAAGTCCGT	GGGCTACGGC
201	TCCTGGTTTG	AGCACGTGCA	GGAGTTCTGG	GAGCACCGCA	TGGACTCGAA
251	CGTGCTTTTT	CTCAAGTATG	AAGACATGCA	TCGGGACCTG	GTGACGATGG
301	TGGAGCAGCT	GGCCAGATTC	CTGGGGGTGT	CCTGTGACAA	GGCCCAGCTG
351	GAAGCCCTGA	CGGAGCACTG	CCACCAGCTG	GTGGACCAGT	GCTGCAACGC
401	TGAGGCCCTG	CCCGTGGGCC	GGGGAAGAGT	TGGGCTGTGG	AAGGACATCT
451	TCACCGTCTC	CATGAATGAG	AAGTTTGACT	TGGTGTATAA	ACAGAAGATG
501	GGAAAGTGTG	ACCTCACGTT	TGACTTTTAT	TTATAATAAC	AGAAACAACA
551	ACCTGCATGC	TCACAATACC	CAGACAGTCT	ACTAGCCAAA	AGTCCTGTAT
601	GCATTCATTT	ATTCCTTGCT	GGACAAACTC	TGGAAGCAGC	GTGTGAAACA
651	GCGGGGGAAG	GGAAGAGCGG	CGTGAGCGGA	${\tt GGGAGTGTGA}$	TGATTCCCAA
701	CCGAAGCAGC	TGTCTCGCCT	TTAGAACGTG	CAGCCTCTCC	ATGTCTGATT
751	ACAAACAGTC	TCCACATTGC	AGTTCCAATG	GCCTGGACCG	TAAGGATAAA
801	GCCTGTAATA	${\tt TATGCAACTA}$	GAATGTCTGC	CTTTTCAACC	CCGTATTATT
851	GTATTTTATA	GAGCTTTTCA	CTGGAAATCT	ACATAAATGT	CAGTAAACCA
901	AATAAAAGTT	CATTTCCAAG	GGGAATCAGG	AGCGAGCCAC	ACCCGAATGG
951	TAGAAAGATC	TCAGGGTTAA	CTCTTTATTT	TTGTAGTTTT	ATTATCTAAG
1001	GCACAGCCAT	TCTGTTCTCA	CTTGGTTCTG	AGATAGTGGT	GAGAACAGAG
1051	GATGAGTTGG	GTCTGTTGGG	GGGAATCTGG	ACACTTGTTT	ATTCTGACGG
1101	AGTTCACTTC	TTCAGAACCT	TCCTGAAATG	AGCAGAAATT	GTTCACTAGG
1151	TCTTCAGAAT	GGACGTCCTT	CTGCCAGAGA	CTTCCAGCGG	GCGGCTCCAA
1201	AGGCCCAATG	CAGAGGAGCC	CGCGGAGCAT	GTGCTGAGGG	AAGTCTGCCT
1251	GGTGAGGCTG		GTCTAATGCA	GTCAGGAGCA	TTTGCATGCA
1301	GTGGGTGGAG	AGTCGGCCAC	CAAAGGACCG	AGTTGCGCTC	GGAATTTGAG
1351	CTGAATTCCA	CAGCCTTACT	TTGTTTCCTG	AAGTGATAGC	CTACTAATGC
1401		ATGCTTAATA	GTAAATTTCT	AAAATCCCCG	GGTCTTTATC
1451	ATTCAGTTTG		CTGAGGCGCT		AGGACCATTT
1501	TGCGAGTGTA	GCCCTGTTTC	ACTCGGATCA	GGTTGGCACG	GCCGCCTGCG
1551	TGTCTGTCCA		CCGTGTATCT		AGGTGAGGTC
1601		CACTGCCTAA	TTTTCTCACC	CACATTCGCT	GAAGCGATGG
1651		GCCAGTAGCC	AGCCAACCCC		GGGTTGTCTG
1701		GGCTGGAAAG	CACCCAAAGT	GGTGGTCAGG	AGGGTCGCTG
1751		GGTCTCCGTT	CTTGGTGCTG	TATTTGAAAC	GGGTGTAGAG
1801	AGAAGCTTGT	GTTTTTGTTT	GTAATGGGGA	GAAGCGTGGC	CAGGCAGGTG
1851	GCACGTGGCA		GGCTCGGCAG	CACCTTGCCT	GTGTTTCTGT
1901	GAGGGAGGCT	GCTTTCTGTG	AAATTTCATT	TATATTTTTC	TATTTTTAGT
1951	ACTGTATGGA	TGTTACTGAG	CACTACACAT	GATCCTTCTG	TGCTTGCTTG
2001	CATCTTTAAT	AAAGACATGT	TCCCGGCGTT	GCAAAAAAAA	AAAAAAAAA
2051	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA		

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Fig. 12: SEQ ID NO. 5

Length: 32 bp

1 GATTGCATCT TTAATAAAGA CATGTTCCCG GC

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Fig. 13: SEQ ID NO. 6: nucleotide sequence of human SULT4A1 coding sequence

Length: 855 bp

1	ATGGCGGAGA	GCGAGGCCGA	GACCCCCAGC	ACCCCGGGGG	AGTTCGAGAG
51	CAAGTACTTC	GAGTTCCATG	GCGTGCGGCT	GCCGCCCTTC	TGCCGCGGGA
101	AGATGGAGGA	GATCGCCAAC	TTCCCGGTGC	GGCCCAGCGA	CGTGTGGATC
151	GTCACCTACC	CCAAGTCCGG	CACCAGCTTG	CTGCAGGAGG	TGGTCTACTT
201	GGTGAGCCAG	GGCGCTGACC	CCGATGAGAT	CGGCTTGATG	AACATCGACG
251	AGCAGCTCCC	GGTCCTGGAG	TACCCACAGC	CGGGCCTGGA	CATCATCAAG
301	GAACTGACCT	CTCCCCGCCT	CATCAAGAGC	CACCTGCCCT	ACCGCTTTCT
351	GCCCTCTGAC	CTCCACAATG	GAGACTCCAA	GGTCATCTAT	ATGGCTCGCA
401	ACCCCAAGGA	TCTGGTGGTG	TCTTATTATC	AGTTCCACCG	CTCTCTGCGG
451	ACCATGAGCT	ACCGAGGCAC	CTTTCAAGAA	TTCTGCCGGA	GGTTTATGAA
501	TGATAAGCTG	GGCTACGGCT	CCTGGTTTGA	GCACGTGCAG	GAGTTCTGGG
551	AGCACCGCAT	GGACTCGAAC	GTGCTTTTTC	TCAAGTATGA	AGACATGCAT
601	CGGGACCTGG	TGACGATGGT	GGAGCAGCTG	GCCAGATTCC	TGGGGGTGTC
651	CTGTGACAAG	GCCCAGCTGG	AAGCCCTGAC	GGAGCACTGC	CACCAGCTGG
701	TGGACCAGTG	CTGCAACGCT	GAGGCCCTGC	CCGTGGGCCG	GGGAAGAGTT
751	GGGCTGTGGA	AGGACATCTT	CACCGTCTCC	ATGAATGAGA	AGTTTGACTT
801	GGTGTATAAA	CAGAAGATGG	GAAAGTGTGA	CCTCACGTTT	GACTTTTATT
851	TATAA	•			

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Fig. 14: Alignment of SEQ ID NO. 5 with human SULT4A1sv1 and SULT4A1sv2 cDNAs

Length: 32 bp

SEQ ID NO.5 : SULT4A1sv1

SEQ ID NO.5 : SULT4A1sv2

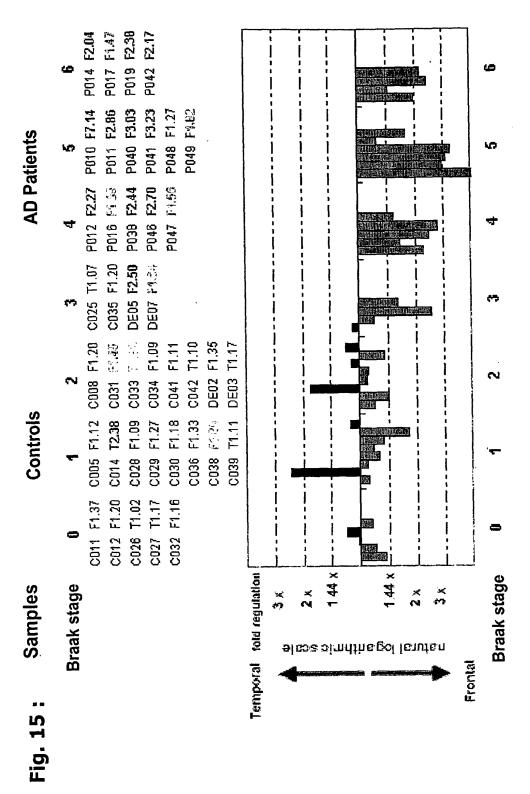
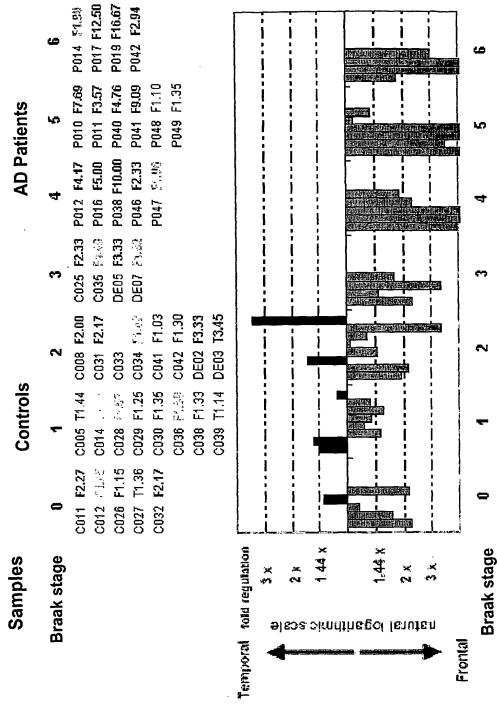


Fig. 16



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AD Patients Log (Ratio HC/IF) (hippocampus/ frontal cortex) 0.050 -0.750 0.550 Log expression: hippocampus / frontal cortex ∆ (fold) 0.82 0.56 0.76 0.13 0.64 0.87 1.37 0.70 0.95 control C004 control C005 control C008 P010 P011 P012 P016 P019 sample patient patient patient patient patient patient

Fig. 1.

SULT4A1 protein in neuroglioma cells Fig. 18: Immunofluorescence analysis of

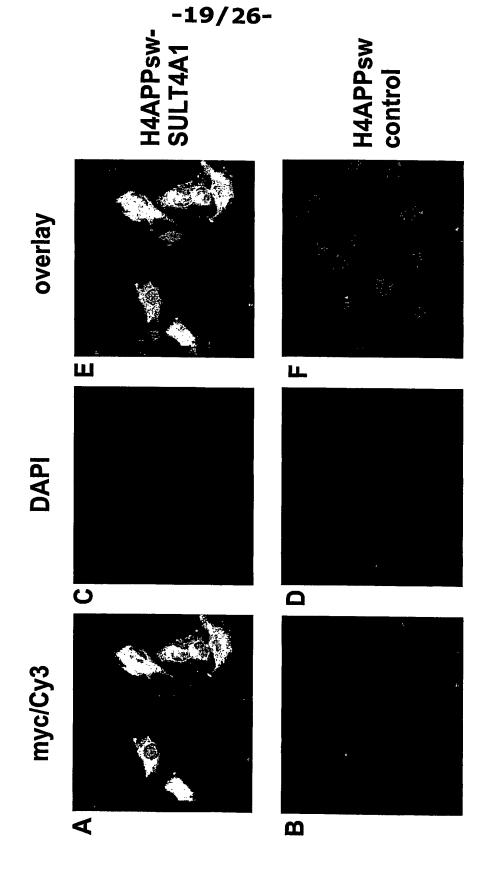


Fig. 19: Effect of trophic factor deprivation on SULT4A1 over-expressing cells

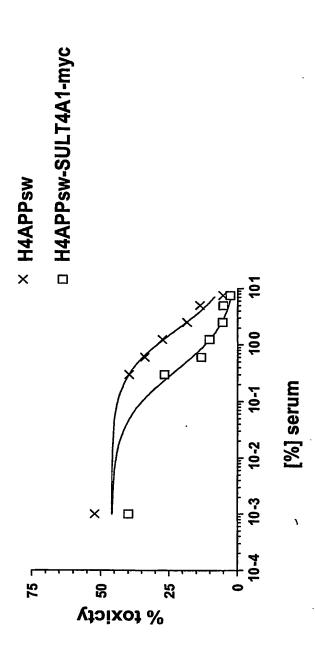


Fig. 20: Generation of Sult4A1 deficient mice

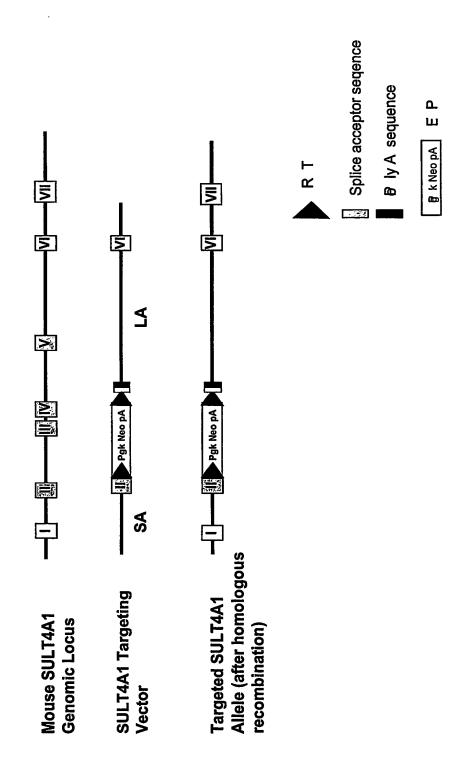
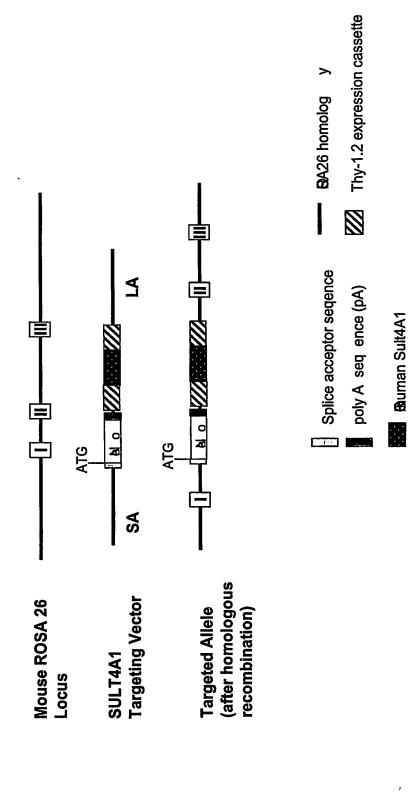


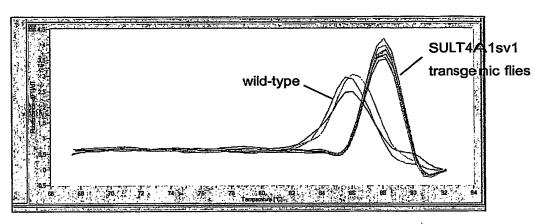
Fig. 21: Generation of Sult4A1 trangenic mice



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Fig. 22: Transgenic expression of Sult4A1

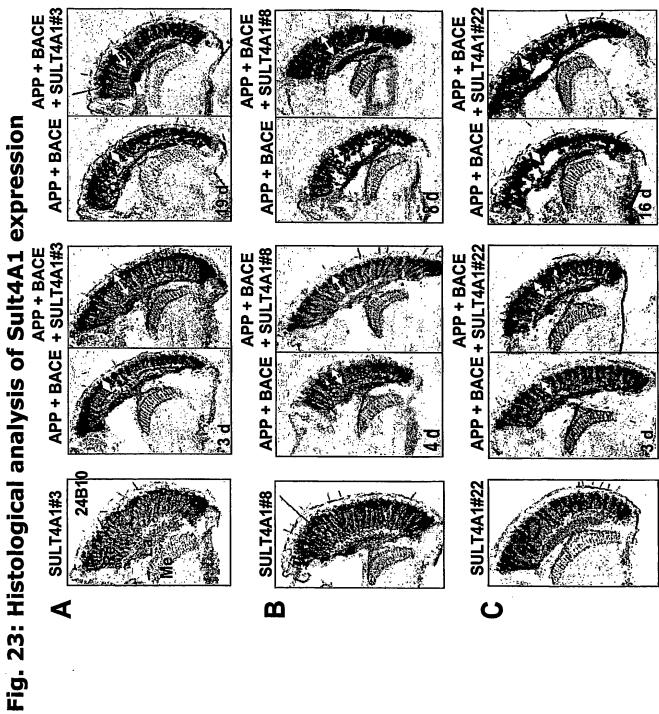
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В

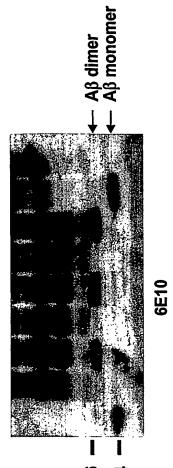
name	cycle number	mean	stdev	error [%]	efficiency (expression normalized to housekeeping gene)	
SULT4A1#3	21.34	21.300	0.14422205	0.67709883	1.8 times more than	
SULT4A1#3	21.14				SULT4A1#8; 2.7 times	
SULT4A1#3	21.42				more than SULT4A1#22	
			•			
SULT4A1#8	23.79	23.917	0.11676187	0.48820292		
SULT4A1#8	23.94					
SULT4A1#8	24.02				~	
SULT4A1#22		23.915	0.03535534	0.1478375		
SULT4A1#22	23.94					
SULT4A1#22	23.89					

E= 10^(-1/slope) slope= -2.960 E= 2.176



wild-type + 3ng AB APP + BACE + SULT4A1#3 **E#IA4TJUS + 99A** Fig. 24: Expression of full-length and processed **APP + BACE ddA** βA gen ε **k**Da \mathbf{m} hAPP in transgenic flies APP + BACE + SULT4A1#3 **E#1A4TJU2 + 99A APP + BACE 44A**

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APPfl

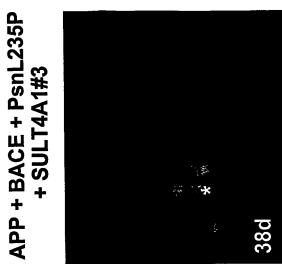
kDa

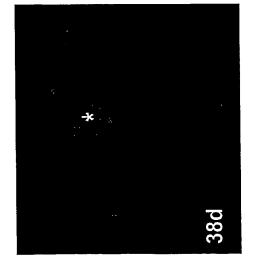
97

Fig. 25: Thioflavin S positive amyloid plaques in transgenic flies

Ω 4

APP + BACE + PsnL235P





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